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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,797	03/15/2000	Athanasius A Anagnostou	5218-39B	9917

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EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	14

DATE MAILED: 04/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/842,700	Anagnostou et al
Examiner	**Art Unit**
Ungar	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 10, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *12-15, 19-21, and 23-26* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *12-15, 19-21, and 23-26* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 10, 2003 has been entered.

2. The Amendment filed on February 10, 2003 (Paper No. 12) and the Declaration filed on February 10, 2003 (Paper No. 13) in response to the Office Action of August 5, 2002 (Paper No. 9) are acknowledged and have been entered. Previously pending claims 17, 18, 22 have been canceled and new claim 26 has been added and claims 12-15, 19, 21 have been amended. Claims 12-15, 19-21, 23-26 are currently being examined.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The following rejections are maintained:

Claim Rejections - 35 USC § 112

5. Claims 13, 15, 23 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in Paper No. 9, Section 5, page 2.

Applicant argues that the Signouas Declaration presents *in vivo* data demonstrating that the instant invention is enabled. The argument has been considered but has not been found persuasive because the claims are drawn to concurrent administration of erythropoietin and administration of erythropoietin after cisplatin. Dr. Signouas states that Group 5, which exemplifies concurrent EPO/CIS

administration, shows a greater reduction in tumor weight than that seen in Group 3, cisplatin alone. However, given, the small number of animals tested, given the close approximation of the tumor weight reduction between Groups 3 and 5, it does not appear and cannot be determined whether or not the differences shown in tumor weight are the result of effective EPO treatment or whether they are the result of normal and expected variation, especially in view of the lack of evidence drawn to a difference in vascularity of the two groups wherein Group 5 is not represented in Figures 1-4. Further, given the wide discrepancy between the concurrent EPO/CIS and CIS alone treatments and the sequential treatment wherein EPO was administered prior to CIS, it cannot be determined, nor could it be predicted that the sequential protocol with CIS being administered prior to EPO would function as claimed, in particular since *in vitro* studies clearly showed that both concurrent EPO/CIS and sequential CIS then EPO resulted in the same biphasic effects of the combined moieties wherein cells cultured with low doses of EPO together with Cisplatin increases the number of viable cells compared with Cisplatin control while simultaneous treatment of cultured cells with high doses high doses of EPO decreases the number of viable cells compared with Cisplatin control. Interestingly, the *in vitro* data of Example 5, in this case, appears to correlate well with the *in vivo* data wherein *in vitro* sequential administration of the moieties, that is prior administration of EPO followed by CIS led to an inhibitory monophasic effect. This appears to be mirrored in the *in vivo* data wherein the effect of this sequential administration protocol led to a tumor size reduction of about twice that of either CIS alone or CIS/EPO concurrent administration. The arguments and the Declaration have not been found persuasive and

the rejection is maintained. Examiner would be happy to consider objective evidence, commensurate in scope with that already submitted for *in vivo* Groups 2-4, but drawn to a comparison of Group 5 with Groups 3 and 4, submitted for the reconsideration of the instant rejection.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. Claims 12, 14, 19-21, 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a solid vascularized tumor in a subject in need of such treatment comprising sequential administration of EPO followed by administration of CIS wherein said erythropoietin is administered in an amount effective to enhance suppression of endothelial growth associated with administration of said cisplatin, does not reasonably provide enablement for a method of treating a solid vascularized tumor in a subject in need of such treatment comprising administering cisplatin in conjunction with erythropoietin wherein said erythropoietin is administered in an amount effect to enhance suppression of endothelial growth associated with administration of said cisplatin, essentially for the reasons set forth previously in Paper No. 7, Section 5, pages 3-10 and Paper No.9, Section 5, page 2) and set forth above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, use the invention commensurate in scope with these claims.

The specification teaches as set forth previously. One cannot extrapolate the teachings of the specification to the enablement of the claims for the reasons previously set forth and those set forth above. The Sigounas Declaration appears to demonstrate

that only sequential administration of EPO followed by CIS is effective to treat a solid vascularized tumor and enhance suppression of endothelial growth associated with administration of said cisplatin. As set forth above, Examiner would be happy to consider objective evidence, commensurate in scope with that already submitted for *in vivo* Groups 2-4, but drawn to a comparison of Group 5 with Groups 3 and 4, submitted for the reconsideration of the instant rejection.

New Grounds of Objection

6. Claims 12-15, 19-20,26 are objected to because claim 12 recites the phrase 'said antineoplastic chemotherapeutic agent". The claim is objected to because there is no antecedent basis in the claim for the phrase. The objection will be withdrawn upon amendment of claim 12, for example, to recite "comprising an antineoplastic agent chemotherapeutic wherein said antineoplastic chemotherapeutic agent is cisplatin" or, for example, to recite "associated with administration of said cisplatin".

7. Claims 23-25 are objected to because claim 23 recites the phrase "with said chemotherapeutic agent" which has no antecedent basis in claim 21 from which it depends. The objection will be withdrawn upon amendment of claims to recite appropriate antecedent basis.

8. All other objections and rejections recited in Paper No. 9 are withdrawn.

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
April 11, 2003